

EXHIBIT 4



Early Child Development and Nutrition: A Review of the Benefits and Challenges of Implementing Integrated Interventions^{1–4}

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ABSTRACT

Poor nutrition (substandard diet quantity and/or quality resulting in under- or overnutrition) and the lack of early learning opportunities contribute to the loss of developmental potential and life-long health and economic disparities among millions of children aged <5 y. Single-sector interventions representing either early child development (ECD) or nutrition have been linked to positive child development and/or nutritional status, and recommendations currently advocate for the development and testing of integrated interventions. We reviewed the theoretical and practical benefits and challenges of implementing integrated nutrition and ECD interventions along with the evidence for best practice and benefit-cost and concluded that the strong theoretical rationale for integration is more nuanced than the questions that the published empirical evidence have addressed. For example, further research is needed to 1) answer questions related to how integrated messaging influences caregiver characteristics such as well-being, knowledge, and behavior and how these influence early child nutrition and development outcomes; 2) understand population and nutritional contexts in which integrated interventions are beneficial; and 3) explore how varying implementation processes influence the efficacy, uptake, and cost-benefit of integrated nutrition and ECD interventions. *Adv Nutr* 2016;7:357–63.

Keywords: early child development, child nutrition, integrated interventions, care, behavior change

Introduction

Poor nutrition (substandard diet quantity and/or quality resulting in under- or overnutrition) and lack of early learning opportunities contribute to the loss of developmental and academic potential and lead to lifelong health and economic disparities in more than 200 million children aged <5 y (1, 2). Moreover, the early provision of optimal nutrition and opportunities for learning (supported by responsive caregiving behaviors that are prompt, contingent on children's actions, and developmentally appropriate and stimulating) have been linked to positive early child development (ECD)⁸ outcomes

(3). ECD typically refers to early childhood with a strong focus on the first 2–3 y of life and describes the gradual unfolding of children's sensory-motor, cognitive-language, and social-emotional capacities shaped by interactions between the environment, experience, and genetics (4).

The 2007 Lancet series on child development in developing countries reported that programs with multiple components, including health, nutrition, and psychosocial stimulation, might be most successful in promoting children's early development (5). Thus, recommendations currently advocate for the development and testing of integrated nutrition and ECD interventions (3, 5). The scientific basis and theoretical framework for integrating nutrition and ECD interventions is discussed in the corresponding review (6), and over the last decade, a substantial number of studies have been undertaken to evaluate the effect of integrated interventions on children's nutrition and development outcomes (7).

In this review, we summarize the current state of knowledge related to the effectiveness of integrated nutrition and ECD interventions, the theoretical and practical benefits and challenges of their implementation, and the emerging evidence for best practices and the cost-benefits. We conclude

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⁸Abbreviations used: BC, benefit-cost; ECD, early child development; SBCC, social and behavior change communication.

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by identifying the current research gaps that need to be addressed to further evidence-based policy and practice for integrated nutrition and ECD programs.

Current Status of Knowledge

Effectiveness of Integrated Early Child Development and Nutrition Interventions

In the last 2 years, systematic reviews and meta-analyses have examined the effectiveness of ECD and nutrition interventions separately (8) and integrated (7) on early child development outcomes. Aboud et al. (8) reviewed interventions conducted since 2000 and found that psychosocial-stimulation interventions ($n = 21$) had a medium-effect size of $d = 0.43$ on children's cognitive development and that nutrition supplementation and education interventions ($n = 18$), had a small-effect size of $d = 0.09$. These findings suggest that integrated nutrition and early child development intervention may have additive or synergistic benefits for child development.

Grantham-McGregor et al. (7) examined the evidence for additive or synergistic benefits to integrated interventions on child development and growth outcomes. They reported that few studies have been designed to address this question and that there was little evidence to support the notion of additive or synergistic benefits to either growth or development outcomes as a result of integrated interventions. However, ECD interventions were consistently found to promote children's development, whereas nutrition interventions were found to benefit children's growth outcomes and sometimes benefit children's development (7).

Given that poor nutrition and inadequate opportunities for early learning are both risks for poor children's development (9, 10), nutritional and ECD inputs should be optimized—and possibly integrated—for best developmental outcomes. However, it is necessary to recognize that integrated interventions must be designed to not only affect a single child outcome but also multiple outcomes, including growth, health, and development. Thus, it is first necessary to review the rationale and feasibility of combining nutrition and ECD interventions to elucidate platforms that might be leveraged for optimizing integration.

The Benefits and Challenges of Implementing Integrated Child Nutrition and Development Interventions

From a program (or health service and systems) perspective, the delivery of integrated nutrition and ECD interventions might well be more efficient than the delivery of separate interventions. Two primary advantages described by DiGironimo et al. (11) were increased access to early learning opportunities for children and the promotion of a comprehensive approach for addressing the whole child. In resource-constrained contexts, integrated services may be an effective strategy for increasing the number of young children and families who are exposed to information and resources that support healthy child growth and development. The colocation of services and use of the same delivery agent might help to address supply-side challenges

in providing adequate access to affordable services. With respect to tackling demand-side challenges, families may find it easier to support the holistic care needs of their young children through a "one-stop-shop" type of service in which information that stems from different interventions is integrated and a relationship with a health worker who understands the total needs of the child and family is established (11).

In addition to program-level advantages, integrated nutrition and ECD interventions support caregiving. Few early childhood interventions that occur within the first 2–3 y of life are child-directed alone but instead target the caregiver-child dyad; for example, the success of an early development intervention depends upon equipping caregivers with the know-how to provide consistent learning opportunities and responsive stimulation for their child within daily routines (12). Similarly, the provision of optimal infant and young children's feeding practices depends upon the caregiver's knowledge and capacity to provide age-appropriate feeding responsiveness and nutritional sufficiency, quality, and diversity. The quality of care provided to young children by their caregivers, typically parents, is the most proximal factor that influences children's survival, health, growth, and development. Early nutrition and development interventions depend on the knowledge, skills, and capacity—both emotional and financial—of caregivers to provide their young child with optimal care for development and nutrition. A growing body of evidence from the disciplines of both nutrition and ECD suggest that there are common skills for effective caregiving and by enhancing these common skills it is possible to benefit outcomes for both nutrition and child development. First, responsive care, or the ability of the caregiver to contingently and appropriately respond to their child's cues, is a skill that needs to be supported for both infant and young child feeding (13–16), as well as supporting healthy social-emotional and cognitive-language development (17). Using the contexts of responsive feeding or play (e.g., responding appropriately to nonverbal and verbal cues of hunger, satiety, and feelings), are both effective ways of supporting responsive caregiving (14, 18).

Second, the low emotional availability of caregivers might challenge the provision of optimal care for nutrition and development for young children. The prevalence of maternal depression is high in low-income (15.9% for pregnant women and 19.8% for postpartum women) and high-income countries (~10.0% for pregnant women and 13.0% for postpartum women) (19) and can compromise the emotional availability of caregivers to recognize and appropriately respond to cues from infants and young children. For example, studies have reported that maternal depression is associated with nonresponsive child-feeding behaviors (20), inadequate and excess dietary intakes (13, 21), and the risk of child under- and overnutrition (22–24).

Furthermore, strategies to promote nutritional well-being and development have incorporated interventions to support the mental well-being of mothers. In Pakistan, the Thinking Healthy program adapted principles of cognitive-behavioral therapy for community health workers to use when counseling

mothers to continue exclusive breastfeeding. The evaluation reported a 60% reduced risk of cessation of exclusive breastfeeding in the first 6 mo of an infant's life (25). In another program, interventions to support maternal well-being were incorporated into a parenting program in Uganda. Parents in the intervention group had significantly lower maternal depressive symptoms than parents in the control group, and the children of parents in the intervention group had significantly higher cognitive development scores compared with children of parents in the control group (26).

A concern surrounding the integration of nutrition and ECD intervention is whether the number of messages becomes ineffective or burdensome for health workers and for families (12, 27). By strengthening common caregiving capacities combined with knowledge about appropriate nutrition and development, integrated messages become potentially more manageable—neither burdening the health worker nor the family. Example messages might include “while breastfeeding your child, you may use the opportunity to sing to your child,” “while feeding your child talk responsively by engaging your child in discussions about the food she is eating,” or “when managing your child's behavior, avoid strategies that include food restriction or rewards.”

There are clear synergies in implementing care for early child nutrition and development together that include leveraging limited supply-side resources, responding to family demand for the provision of holistic care, and leveraging common caregiving competencies to support early child nutrition and development outcomes. Although addressing limited supply-side resources may be especially advantageous in low-income contexts, the provision of integrated care and common caregiving competencies may also be advantageous in middle- and high-income contexts in which issues of over-nutrition (and early care/feeding practices related to overnutrition, such as feeding in the absence of hunger) are becoming increasingly problematic or already exist. However, in populations where poverty and food insecurity is high (resulting in micronutrient deficiencies, stunting, and wasting), the points of integration may not only include common caregiving competencies and knowledge on nutrition and ECD but may also necessitate nutritional supplementation.

In summary, integrated approaches that include a focus on the child (stimulation and nutrition), the parent (maternal depression), and the parent-child relationship (knowledge and responsive care skills for feeding, play, and communication) may well be more effective and sustainable than approaches that consider the child with little attention to the family care context. However, to optimize the effectiveness of integrated interventions, more research is necessary to understand both the combined effect and the effect of individual interventions on a broad range of outcomes related to the delivery of care for children's nutrition and development (e.g., reduction in maternal depressive symptoms and enhancement in responsive care and feeding behaviors) and how these variables might mediate young children's nutrition and development outcomes. For example, research is needed to understand how theoretical frameworks of care that combine

varying nutrition and development messages might be best aligned and delivered. These messages and delivery strategies have to be reflected in common curricula, training materials, supervision, behavioral change techniques, and delivery practices.

Lessons Learned for Successful Implementation of Child Nutrition and Development Interventions

Best practice in nutrition interventions. Appropriate delivery techniques and platforms are critical to the success of nutrition interventions. Best practices for child nutrition interventions include the provision of evidence-based nutrition-specific interventions that address the immediate causes of under- or overnutrition for infant and young children (28), social and behavior change communication (SBCC) strategies (29–31), and nutrition-sensitive interventions that draw on complementary sectors such as agriculture, social safety nets, early child development, and schooling to affect the underlying determinants of poor nutrition, including limited access to healthy foods and lack of adequate care (32).

The recent Lancet series on maternal and child nutrition reported that a substantial reduction in the burden of undernutrition could be achieved if low-income populations had access to 10 evidence-based nutrition-specific interventions (28). The interventions target maternal nutrition during pregnancy (multiple micronutrients, use of iodized salt, calcium intake, and balanced energy protein supplementation), infant and young child nutrition [promotion of optimal infant and young child-feeding practices, food, and micronutrient supplementation (zinc and vitamin A)], and the management of acute malnutrition (28). Evidence-based prevention of childhood overweight/obesity demonstrates that interventions should target children early in life and should focus on improving dietary quality, care/feeding practices, and physical activity (33, 34).

The promotion of healthy dietary patterns and feeding behaviors and the success of these interventions require the implementation of SBCC strategies that target behavior change among those who directly (parents) or indirectly (family and community members) influence child nutrition outcomes (31, 35). SBCC uses communication techniques to help change behaviors by a process of providing individuals with relevant behavior change messages through an interactive and culturally appropriate mix of individuals, groups, and media contacts. A review of 6 SBCC complementary feeding interventions in low- and middle-income countries found that complementary feeding interventions that used 3–4 (out of 6) behavior change techniques were most successful at improving child feeding, diet, and growth outcomes (29). Techniques included the provision of 1) structured information and instruction; 2) performance activities (modeling healthy eating, practice, feedback, and positive reinforcement); 3) problem solving (identifying facilitators and barriers to behavior change and solutions to reducing barriers); 4) social support (peer, community, and authority support); 5) material (nutritional supplements); and 6) small media (songs, role plays, pictures, flash cards, and posters) (29). However, the details and fidelity surrounding the implementation of SBCC

techniques are often not reported in the nutrition intervention literature.

Finally, the success and sustainability of nutrition interventions also require the implementation of large-scale nutrition-sensitive interventions developed to address the underlying determinant of nutrition risk, extending from poor agriculture practices, poverty, and gender inequality to household factors such as mealtime organization and responsive caregiving and feeding behaviors (32, 3).

Best practice in child development interventions. Yousafzai et al. (12) reviewed 31 studies that delivered integrated early childhood interventions and identified several key features associated with successful programs. Common features included the use of a structured curriculum (e.g., organized by developmental stages), use of low-cost materials (e.g., homemade toys), and opportunities for parents to practice play (stimulation) activities with their young children and receive feedback on how the interaction might be strengthened as well as opportunities for problem solving. Both individual contacts through home visit programs and group contacts through parenting groups were reviewed. Few studies, to our knowledge, have explored dosage, but in general fortnightly home visits lasting 30–60 min were reported in successful interventions. Compliance was generally high in home visit programs but variable in parenting groups (lower compliance in longer-duration programs and a higher compliance in shorter, more intense programs).

Behavior change techniques used in early child development interventions have also been reviewed. In a systematic review of 21 studies, Briscoe and Aboud (29) categorized the types of SBCC techniques used in the interventions (using the same list of techniques described previously), namely structured information and instruction, performance activities, problem solving, social support, and small media; similar to the finding for the complementary feeding studies, they reported that the greater the number of SBCC applied the more effective the intervention was at improving young children's cognitive development ($r = 0.44$, $P < 0.05$). Individually, the 3 techniques with the strongest correlation to children's cognitive outcomes were the use of small media ($r = 0.51$, $P < 0.05$), performance-based techniques ($r = 0.34$, $P < 0.12$), and problem solving ($r = 0.34$, $P < 0.12$); however, the numbers of studies that reported these techniques for correlation analyses was very small (8).

Finally, similar to nutrition-sensitive approaches, supporting the broader capacity of the family to provide optimal care for their young children is likely to benefit early child development. For example, conditional cash transfer programs, with conditions linked to attendance at well-child visits or enrollment in preschool centers, have been shown to benefit children's growth and development through 2 potential pathways (36). First, families may invest in better nutrition for their young children and in learning/play materials. For example, mothers who received a nonconditional cash transfer in Ecuador were likely to purchase a toy for their young child. Second, reduced financial pressure

and stress may lead to improved psychosocial well-being in the family and thus improved early child care practices (37).

Synergies for implementing integrated child nutrition and development interventions. Common themes dictate best practices (or the practices that are associated with positive outcomes) for both nutrition and child development interventions. These themes include common recipients, the inclusion of both intervention-specific (e.g., provision of nutrition supplements and low-cost play material) and intervention-sensitive strategies (e.g., promotion of positive maternal mental health and economic opportunities), and the provision theoretically based on SBCC techniques that promote positive caregiving behaviors (Table 1) (38–46).

However, despite similarities across child nutrition and development intervention, the best practices for implementing integrated nutrition and development interventions are poorly understood. Recent reviews of efficacy trials have failed to find combined effects of integrated interventions (7), and at least 2 studies have reported dilution of independent growth (27) and development (39) effects when combining community-based, integrated interventions. The apparent lack of synergy and possible diluted effects may stem from a deviation from best practices with an attempt to deliver too many behavior change messages, thereby weakening the community-based delivery platform and the caregivers' ability to absorb and practice all the recommended messages.

Evidence for Benefit-Cost Analysis of Integrated Child Nutrition and Development Interventions

If optimizing alignment of care for nutrition and child development delivery practices is effective, we must also consider whether it is feasible and beneficial to programs with respect to cost. Evidence for the benefit-cost (BC) of integrated nutrition and child development programs is currently limited (46–49).

BC analyses allow for the assessment of different alternatives of investments across different types of interventions or multiple outcomes. They provide policymakers with the necessary information to quantify the economic returns to their policies. Integrated nutrition and child development interventions could have an array of impacts, including improvements in nutritional status, cognitive development, academic achievement, labor market outcomes, and crime reduction. To calculate BC, the costs of service providers (including wages and training), material cost, and rental price of space and utilities need to be measured. Private costs, such as time and transportation incurred by mothers, are difficult to measure because data are not always available. Alderman et al. (50) presented methodology on how to measure BC ratios of integrated programs, including issues such as using comparable units of measurement, avoiding double counting, considering dynamic effects, accounting for private and social returns, and the fact that benefits might not constantly depend on, for instance, the age of the child. Figure 1 shows a summary of the current status of evidence for BC ratios of integrated child nutrition and development

TABLE 1 Similarities and differences in best practices across nutrition and ECD interventions¹

	Best practice in nutrition	Best practice in ECD
Recipients	Adolescent females, women of reproductive age, pregnant women, neonates, and infants and young children (28)	Caregivers, infants, and preschool-aged children through school entry (3)
Intervention-specific strategies ²	Provision of health care, nutrition education, and nutrition supplements	Parenting education and support on a range of topics (e.g., importance of play and communication, positive discipline, practices, school readiness, providing support to mothers and fathers) and provision of play material and books (homemade, low-cost, or via book and toy libraries)
Intervention-sensitive strategies ³	Agriculture (including biofortification and home-gardening) (32); social safety nets (including conditional and unconditional cash transfers, school feeding programs, household food distributions, and emergency assistance programs) (32); ECD (13, 38); schooling (32)	Social safety nets (including conditional and unconditional cash transfers (36, 37); nutrition (education, including responsive feeding, and supplements) (38, 39)
SBCC techniques	Information and instruction: communicating information and verbal instruction about responsive feeding and optimal feeding practices (type, frequency, and preparation of infant foods) (40–45) Performance activities: modeling, practicing, and providing feedback for responsive feeding (40); modeling optimal feeding practices (amount, frequency, and preparation of infant foods) (41–45) Problem solving: identifying barriers and solutions to support responsive feeding and optimal feeding practices (40, 41) Social support: encouraging peer (40), community (41), and authority (44) support, and support for responsive feeding and optimal feeding practices (type and amount of infant foods) Material: provision of nutritional supplements (38, 39) Small media: illustrating responsive feeding and optimal feeding practices (amount, frequency, and preparation of infant foods) via pictures, flipcharts, and posters (8, 13, 38)	Information and instruction: communicating information and verbal instruction about what caregivers should do with their children and why (8) Performance activities: demonstrating and practicing with feedback about how to talk and play with children (8, 12) Problem solving: addressing maternal depression, need for family support, lack of time, lack of resources, and not knowing how to talk to infants (8, 12) Social support: encouraging family support during intervention home visits and facilitating peer groups (8, 12) Material: play material (e.g., homemade, low-cost, or via toy and book libraries) (8, 12) Small media: illustrating stimulation practices via posters, video, and discussion (8, 12)

¹ ECD, early child development; SBCC, social and behavior change communication.

² Interventions that address the immediate causes of poor outcomes.

³ Interventions that address the underlying causes of poor outcomes.

interventions across 4 different studies (conducted in Nicaragua, Colombia, Bolivia, and Jamaica). All studies tended to have large sample sizes, ranging from 600 (49) to >10,000 (47). All programs had components of nutrition or health and child development combined, so it is not possible to tease out their independent effects. The programs in Nicaragua, Colombia, and Bolivia included a center-based component of either full-day care or preschool, some of which were in the caregiver's home (46–48).

Beyond the synergies in impacts, the integration of nutrition and ECD might lead to cost savings from joint implementation. However, the evidence base is too limited to reach clear conclusions. Still, there are positive examples from Jamaica, even when considering the attenuation of benefits at scale. One of the potential benefits of integrating ECD services into the health sector is the potential for lower costs as a result of synchronized training, monitoring and supervision, and the use of the same personnel. However, whether

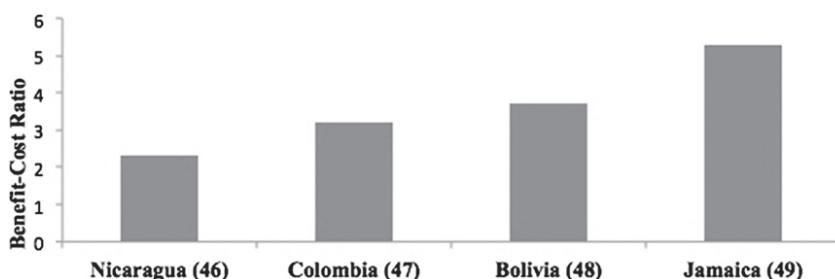


FIGURE 1 Benefit-cost ratios for integrated programs to improve child development outcomes. The benefit-cost ratios are calculated by dividing the total discounted present value of the benefits of a program over the life course of an individual by the total discounted costs over the total duration of the program. Both are expressed in monetary terms.

there will be a negative or positive impact on the existing personnel and service is unknown.

Conclusions

In summary, the strong theoretical rationale for integration is more nuanced than the questions that the past empirical evidence has addressed and thus places greater emphasis on a child and family approach and a need for studies that allow us to examine important questions of mediation, moderation, implementation, and cost. For example, further research is needed to 1) answer questions related to how integrated messaging influences caregiver characteristics such as well-being, knowledge, and behavior and how these characteristics influence early child nutrition and development outcomes; 2) understand population and nutritional contexts in which integrated interventions are beneficial; and 3) explore how varying implementation processes influence the efficacy, uptake, and cost-benefit of integrated nutrition and ECD interventions.

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